

REMARKS

The Examiner has revoked allowability for Claims 22-25 and 27-31 and asserted a number of rejections and they are addressed in the order presented below.

I. Rejections Under 35 U.S.C. § 103(a)

A. Claims 22-25 and 27-31 are allegedly being unpatentable over Ecke et al, *Intl J Eng Sci* 36:1471-1480 (1998), in view of Vorobieff et al. *Physica D* 123:153-160 (1998), and further in view of Selvaganapathy et al., *Proc IEEE* 91:954-975 (2003).

B. Claims 22-25 and 27-31 are allegedly being unpatentable over *United States Patent Application Publication No. 2003/0077599* To Sogard in view of *United States Patent No. 5,169,918* To Tomishima et al.

With the exception of Tomishima et al., the Applicants point out that the Examiner had all of the cited references when allowing Claims 22-25 and 27-31.¹ In view of this unexpected, and somewhat questionable development, the Applicants present new Claims 32 – 54. The argument presented below regarding Claims 22-25 and 27-31 apply equally to the examination of new Claims 32 – 54.

I. The Claims Are Not Obvious

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP* § 2142; Establishing A *Prima Facie* Case Of Obviousness. The Examiner is reminded that

¹ The Examiner had an opportunity to provide Rejection IA in the previous Office Action, but instead allowed the Claims.

if ONLY ONE of the above requirements is not met, then a *prima facie* case of obviousness does not exist. The Applicants submit that the Examiner's rejection does not meet these criteria. The Applicants rebut the establishment of a *prima facie* case of obviousness by the argument below.

A. Ecke et al. And Vorobieff et al. Do Not Teach The Claimed Embodiment

The Examiner has admitted that Ecke et al. and Vorobieff et al.:

... do not teach wherein the solution introduced into the reaction vessel comprises a plurality of reactants, wherein said reactants comprise nucleic acid ...

Office Action, pg. 4. Indeed, Ecke et al. and Vorobieff et al. are theoretical physics references and do not discuss any practical applications of convection cells. Further, the Examiner is requested to note that the aspect ratio defined in Ecke et al. is not the same aspect ratio as defined by the Applicants. The Examiner states that Ecke's aspect ratio is radius-to-height (i.e., for example, r/h). *Office Action, pg. 3, last sentence.* The Examiner is requested to compare this with the Applicants' aspect ratio definition:

In one embodiment, the reaction chamber has, for example, an aspect ratio (h/d , where h =height and d =diameter) ...

Applicants' Specification, pg. 3 ln 28-29. Ecke's aspect ratio and the Applicants' aspect ratio are inversely related. The Examiner should realize that, for example, a reaction vessel having an aspect ratio of 3.3 would be wide & short under Ecke's definition, but would be narrow and long under the Applicants' definition.

B. Selvaganapathy et al. Is Not Prior Art

The Examiner then attempts to link Ecke et al./Vorobieff et al. with Selvaganapathy et al. by stating that:

Selvaganapathy et al. teach that the use of naturally developed Raleigh-Benard convection between two regions of differing temperature may be used for performing PCR ...

Office Action pg 4. The Examiner has, apparently, overlooked the cited reference [16] within Selvaganapathy et al. which supports the Examiner's conclusion. The Applicants provide below the entire passage, in context, for discussion purposes:

Instead of using artificial pneumatic movement, naturally developed Raleigh-Bernard convection between two regions of differing temperature has also been used for performing PCR [16].

Selvaganapathy et al., pg 955 rhc. Reference [16] within Selvaganapathy et al. is:

M. Krishnan, V. Ugaz, and M.A. Burns, "PCR in a Rayleigh Bernard convection cell" *Science* vol. 298, pp. 793-794, 2002.

Selvaganapathy et al., pg. 972, lhc. The Examiner is requested to note that the authors of Selvaganapathy's reference [16] are the same as the inventors of the claimed invention. The Applicants argue that the Krishnan et al. *Science* publication provides evidence of prior conception and reduction to practice regarding this passage within Selvaganapathy et al. Consequently, for the proposition advanced by the Examiner, Selvaganapathy et al. cannot be considered prior art.

As a supplementary matter, the Applicants provide a 37 CFR 1.131 Declaration signed by all the inventors "swearing behind" the 2002 *Science* publication as a potential 35 U.S.C. § 102(a) reference.²

In conclusion, since Ecke et al. and Vorobieff et al. do not teach most of the claimed elements, and Selvaganapathy et al. is not proper prior art the Applicants respectfully request that the Examiner withdraw the present rejection.

B. The Claims Are Patentable Under Sogard and Tomishima et al.

1. Tomishima et al. Is Non-Analogous Art

The Examiner has tried to justify revoking the allowability of Claims 22-25 and 27-31 by adding Tomishima et al. as a new reference. Tomishima et al. is directed

² This Science paper was published after October 3, 2002.

towards plastics technology³ and not biological technology. Consequently, the Applicants submit that Tomishima et al. is non-analogous art.

The Federal Circuit has outlined a basic definition for non-analogous art:

The determination whether prior art is analogous involves some factual issues concerning whether the reference is within the field of the inventor's endeavor or reasonably pertinent to the particular problem with which the invention was involved.

Finish Engineering Co., Inc. v. Zerpa Industries, Inc., 806 F.2d 1041, 1 USPQ2d 1114, 1116 (Fed. Cir. 1986). Because the Applicants have ordinary skill in biology they would not be motivated to consider references in plastics. Consequently, Tomishima et al. is not “within the field of the inventor’s endeavor”.

The Applicants argue that Tomishima et al. also is not “reasonably pertinent to the particular problem to which the invention was involved”. The Examiner is reminded that this determination is made from the viewpoint of one having ordinary skill in the art:

A reference is reasonably pertinent if ... [it] ... logically would have commended itself to an inventor’s attention in considering his problem.

In re Clay, 966 F.2d 656, 659-660 (Fed. Cir. 1992)(citing *In re Deminski*, 796 F.2d 436 (Fed. Cir. 1986). The determination of whether an inventor would consider a specific reference is based upon the expressed purpose of the reference:

If a reference disclosure has the same purpose as the claimed invention, the reference relates to the same problem ... If it is directed to a different purpose, the inventor would accordingly have had less motivation or occasion to consider it.

Id. In addition, Tomishima et al. and the Applicants’ presently claimed embodiment do not solve the same problem. The Applicants submit that a person having ordinary skill in the art would not reasonably have expected to solve the Applicants’ problem of moving reactants between a high temperature region and low temperature region within the same

³ Tomishima et al. teaches vinyl chloride polymerization.

vessel by considering Tomishima et al. that deals with maintaining reactants at a uniform temperature within the same vessel (*infra*).

Consequently, the Applicants respectfully request that the Examiner withdraw the present rejection.

2. There Is No Motivation To Combine The Teachings Of Sogard With Tomishima et al.

Even if the Examiner disagrees that Tomishima et al. is non-analogous art (even though it is) the rejection still fails because there is no motivation for one having ordinary skill in the art to combine the teachings of Sogard and Tomishima et al.

The Examiner concludes that:

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to modify the apparatus of Sogard to encompass an aspect ratio of at least 3.3 ... as taught by Tomishima et al.

Office Action pg 6. The Applicants disagree because Sogard makes no mention of any desirability to modify an aspect ratio. In fact, Sogard makes no mention of an aspect ratio whatsoever. The Examiner is reminded that suggestions and motivations to modify a reference must come from one having ordinary skill in the art, and not the Examiner:

The mere fact that the prior art could be modified in the manner proposed by the Examiner would not have made the modification obvious unless the prior art suggested the desirability of the modification.

Ex parte Dussard, 7 USPQ2d 1818, 1820 (Bd. Pat. App. & Int., 1988). Consequently, one having ordinary skill in the art, upon reading Sogard would not be motivated to seek Tomishima et al. in order to consider modifying an aspect ratio.

The Examiner is asked to take note of the recent Supreme Court opinion which says that a specific showing by the Examiner is required:

Often, it will be necessary ... to look to interrelated teachings of multiple patents ... in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate

review, this analysis should be made explicit. See, *In re Kahn*, 441 F.3d 977, 988 (CA Fed. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”).

KSR v. Teleflex, Slip Op No. 04-1350 (April 30, 2007). Further, Sogard teaches that Rayleigh-Benard convection cells may interfere with DNA hybridization and advocates the elimination of convection cells:

When the lower surface is warmer than the upper surface, one might expect formation of Rayleigh-Benard convection cells ... This may affect either the hybridization rate or the achievable stringency. However the onset of the Rayleigh-Benard instability is retarded when the separation between the upper and lower surfaces is small, and when the temperature difference is small. Therefore Rayleigh-Benard convection may be absent ...

Sogard, pg 4, para [0043] [emphasis added]. Sogard, therefore, specifically “teaches away” from Tomishima’s methods and, if anything, suggests using reaction vessels with small h/d aspect ratios.

3. Sogard and Tomishima et al. Fail To Teach All The Claimed Elements

Even if the Examiner decides that Sogard and Tomishima et al. are properly combined (which they are not) the present rejection still fails because the combined references fail to teach all the claimed elements. Neither reference teaches “thermocycling of reactants” within a reaction vessel to form a reactant product. In fact, Tomishima et al. explicitly states that their invention solves a problem related to a non-uniform temperature distribution within a reaction vessel:

... the temperature in the apparatus differs between the upper and lower parts of the apparatus when conventional temperature-control systems are employed, and the resulting polymer particles have a wide distribution of polymerization degrees. ... It has been found that the above problem can be solved by dividing the jacket of the polymerization apparatus and cooling the upper part thereof, thereby generating mixing flows in the upward and downward directions by means of natural convection to create a uniform temperature distribution.

Tomishima et al., col 6 ln 61 – col 7 ln 24 [emphasis added]. Clearly, Tomishima et al. teaches a reaction vessel having a single uniform temperature, not a reaction vessel having distinct temperature areas (i.e., for example, a vessel capable of supporting thermocycling).

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claim 22 to recite that the convection cell comprises “a temperature differential” thereby resulting in “thermocycling” of the reactants⁴. These amendments are made not to acquiesce to the Examiner's argument but only to further the Applicants' business interests, better define one embodiment and expedite the prosecution of this application.

CONCLUSION

The Applicants believe that the arguments and claim cancellations set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. The remaining claims are, therefore, in condition for allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.984.0616.

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⁴ The Examiner is requested to note that “thermocycling” appears in each independent claim.